(P 395) Transport of Small Anionic and Neutral Solutes Through Chitosan Membranes: Dependence on Crosslinking and Chelation of Divalent Cations

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Chitosan membranes were prepared by solvent casting and crosslinked with glutaraldehyde at several ratios under homogenous conditions. The crosslinking degree varying from 0 to 20% is defined as the ratio between the total aldehyde groups and the amine groups of chitosan. Permeability experiments were conducted using a side-by-side diffusion cell to determine the flux of small molecules of similar size, but holding different chemical moieties, either ionised (benzoic acid, salicylic acid and phthalic acid) or neutral (2-phenylethanol) at physiological pH. The permeability of the different model molecules revealed to be dependent on the affinity of those structurally similar molecules to chitosan, i.e., related to the partition coefficient determined in an independent experiment. The permeability of the salicylate anion was enhanced by the presence of metal cations commonly present in biological fluids, such as calcium and magnesium, but remained unchanged

for the neutral 2-phenylethanol. This effect was explained by the chelation of metal cations on the amine groups of chitosan, which increased the partition coefficient. The crosslinking degree was also correlated with the permeability and partition coefficient. The change in the permeation properties of chitosan to anionic solutes in the presence of these metallic cations is an important result and should be taken into consideration in the *in vitro* predictions of the drug release from chitosan based controlled drug release systems.